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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/877,935	06/08/2001	Daniel Pinto	13294-002001	1394

26191 7590 06/28/2005

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EXAMINER	
QIAN, CELINE X	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 06/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/877,935	PINTO ET AL.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-12,32,33 and 35-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,3-6,8-12,32,35,36,41 and 43* is/are allowed.

6)☒ Claim(s) *33,37-40 and 42* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-6, 8-12, 32, 33, 35-43 are pending in the application.

This Office Action is in response to the Amendment filed on 4/13/05.

Response to Amendment

The rejection of claims 1, 11, 12, 36 and 41 under 35 U.S.C.102 (b) has been withdrawn in light of Applicant's amendment of the claims.

The rejection of claims 1, 10-12, 42 and 43 under 35 U.S.C. 112 1st paragraph has been withdrawn in light of Applicant's amendment of the claims.

The rejection of claims 9, 10, 35, 39 and 40 under 35 U.S.C. 112 2nd paragraph has been withdrawn in light of Applicant's amendment of the claims.

The rejection of claim 33 under 35 U.S.C.112 1st paragraph is maintained for reasons set forth in the previous office action mailed on 1/11/05 and further discussed below.

Claims 37-40 are rejected under 35 U.S.C. 112 1st paragraph for reasons discussed below.

Claim 42 is rejected under 35 U.S.C. 112 2nd paragraph for reasons discussed below.

Claim 2 is objected to for reasons discussed below.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described

in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In response to the written description rejection applied to previous claims 1, 10-12, 33, 42 and 43, Applicants amended claims 1, 42 and 43 to recite the new limitation SEQ ID NO:1. Applicants assert that the amendment overcome the rejection of the record.

The examiner agrees with Applicants that this rejection is overcome by such amendment as applied to claims 1, 42, 43, and depending claims 10-12. However, claims 33 still recites a sequence which is the sequence extending 5.5kb upstream and 3.5kb downstream from the transcription initiation site, which is not disclosed in the specification for having any promoter activity. As discussed in the previous office action, the specification only discloses a 9kb fragment of SEQ ID NO:1 comprising sequence extending 3.5kb upstream and 5.5kb downstream from the transcription start site, and fragments within this sequence having villin gene promoter activity. The nucleotide sequence recited in claim 33 clearly comprises sequence more upstream than that encompassed in SEQ ID NO:1, and missing the HS II and I site within SEQ ID NO:1. As such, the specification does not provide sufficient written description for the claimed nucleotide sequence. This rejection is thus maintained.

New Grounds of Rejection Necessitated by Applicant's Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the isolated nucleotide sequence comprising a nucleotide fragment extending from the nucleotide position –100 or -480 upstream from the transcription initiation site, to the translation initiation site; the sequence extending from the translation initiation site of murine villin gene upstream to a sequence that is 3.5kb upstream from the transcription initiation site, wherein the intron 1 region is deleted; and the sequence of SEQ ID NO:1 and fragments thereof mutated by deletion of one or several nucleotides within the intron 1 region, but not the HS II Dnase I hypersensitive site, wherein said sequences promotes the transcription and tissue-specific expression of the murine villin gene in intestine epithelial cells and kidney proximal tubules *in vitro*, does not reasonably provide enablement for these fragments wherein said sequences promotes the transcription and tissue-specific expression of the murine villin gene in intestine epithelial cells and kidney proximal tubules *in vivo* (ie., in transgenic mouse). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

The nature of the invention is isolated nucleotide sequences comprising a nucleotide fragment extending from the nucleotide position –100 or -480 upstream from the transcription initiation site, to the translation initiation site; the sequence extending from the translation initiation site of murine villin gene upstream to a sequence that is 3.5kb upstream from the transcription initiation site, wherein the intron 1 region is deleted; and the sequence of SEQ ID NO:1 and fragments thereof mutated by deletion of one or several nucleotides within the intron 1 region, but not the HS II Dnase I hypersensitive site, wherein said sequences promotes the transcription and tissue-specific expression of the murine villin gene in intestine epithelial cells and kidney proximal tubules.

The breadth of the claims encompasses the claimed nucleotide sequences, which can promote the transcription and tissue-specific expression of the murine villin gene in intestine epithelial cells and kidney proximal tubules both *in vitro* and *in vivo*. According to the disclosure of the specification, the claimed nucleotide sequences can direct the transcription and tissue-specific expression of the murine villin gene in intestine epithelial cells and kidney proximal tubules cell lines in vitro (CaCo2 and LLCPK1, see Figure 3). However, such nucleotides clearly do not have such function *in vivo*, for example, in the transgenic mouse studies performed by Applicants. The specification discloses that the sequence extending from the nucleotide position –100 or -480 upstream from the transcription initiation site, to the translation initiation site cannot direct intestine and kidney specific gene expression in transgenic mouse study (see Figure 7, and page 23-24). The specification also teach that the sequence comprising SEQ ID NO:1 with intron deletion can only direct gene expression in intestine, but not kidney in transgenic mouse (see Figure 7, page 24). The prior art is silent on sequences from

5' of the murine villin gene which can direct tissue specific expression in intestinal epithelial cells and kidney proximal tubule cells. As such, one skilled in the art would have to rely on the teaching of the specification to use the invention as claimed. As the disclosure of the specification only enables the promoter activity in intestinal epithelial cells and kidney proximal tubule cells *in vitro*, the skilled artisan would have to engage in undue experimentation to make and use the claimed invention in commensurate with the scope of the claims. Therefore, the claimed invention is only enabled to the scope as indicated above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 42, the recitation of "a nucleotide fragment extending from an HS1 hypersensitive site downstream to an HS IV Dnase I-hypersensitive site and extending from –1kb to 5.5kb with respect to the transcription initiation site of SEQ ID NO:1" renders the claim indefinite because it is unclear which fragment Applicants are referring to. According to the disclosure of the specification, HS I hypersensitive site is at approximately 5.5kb from the transcription start site, whereas HS IV hypersensitive site is at approximately –1kb from the transcription start site. It appears that the recited fragment comprises overlapping sequence, and the boundary of the claimed sequence cannot be determined. As such, the metes and bounds of the claim cannot be established.

Claim Objections

Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 2 recites "the sequence extending 5.5kb upstream and 3.5kb downstream from the transcription initiation site of the murine villin gene." The sequence of SEQ ID NO:1 recited in claim 1 is the sequence extending 3.5kb upstream and 5.5kb downstream from the transcription initiation site of the murine villin gene, which does not encompass the sequence extending 5.5kb upstream and 3.5kb downstream from the transcription initiation site of the murine villin gene. Nor does fragments of SEQ ID NO:1 encompass said sequences. Thus, claim 2 fails to further limit claim 1.

Conclusion

Claims 1, 3-6, 8-12, 32, 35, 36, 41 and 43 are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

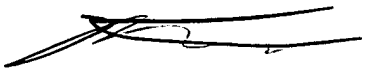
CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CELIAN QIAN
PATENT EXAMINER



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Art Unit 1636